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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/705,500	11/03/2000	Herve Recipon	DEX-0087	6616

7590 10/08/2003

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	23

DATE MAILED: 10/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/705,500	Applicant(s) RECIPON ET AL.	
	Examin r Karen A Canella	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-5 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-5 have been amended. Claims 1-5 and 12 are pending and under consideration. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

2. The rejection of claims 1, 2 and 12 under 35 U.S.C. 102(e) as being anticipated by Olsen et al (Pub No. US 2002/0042372 A, priority to October 27, 1999) as evidenced by the alignment of the instant amino acid sequence of SEQ ID NO:3 and polynucleotide of Sequence 1 is maintained for reasons of record.

Claim 1 is drawn to a method for diagnosing the presence of cancer in a patient comprising determining the level of Lng108 in cells, tissues or bodily fluids in a patient; and comprising the determined levels of Lng108 with levels of Lng108 in cells, tissues or bodily fluids from a normal human control, wherein a change in determined levels of Lng108 in said patient versus normal human control is associated with the presence of cancer and wherein Lng108 comprises a polynucleotide of SEQ ID NO:1 or 2, a polynucleotide which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO:1 or 2, or a protein expressed by a polynucleotide sequence of SEQ ID NO:1 or 2. Claim 2 is drawn to a method of diagnosing metastases of cancer in a patient comprising determining Lng108 levels in a sample of cells, tissues or bodily fluids from a patient; and comprising said Lng108 levels with the Lng108 levels in the cells, tissues or bodily fluids of a normal human control, wherein an increase in the Lng108 levels in said patient is associated with a cancer which has metastasized, and wherein Lng108 comprises a polynucleotide of SEQ ID NO:1 or 2, a polynucleotide which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO:1 or 2, or a protein expressed by a polynucleotide sequence of SEQ ID NO:1 or 2. . Claim 12 is drawn in part to the methods of claims 1 and 2 wherein the cancer is lung cancer.

Olsen et al disclose methods of detecting cancer and metastatic cancer comprising detecting stanniocalcin [0382, 0400, 0402, 0421, 0427, 0428]. Olsen et al specifically disclose the detection of metastases of lung carcinoma ([0428] "Additionally diseases or conditions associated with increased cell survival that could be ...detected by stanniocalcin polynucleotides or polypeptides...include but are not limited to progression and/or metastasis of malignancies

...such as leukemia and solid tumors including...lung carcinoma [and] small cell lung carcinoma...".

3. Applicant argues that the disclosure of Olsen et al does not enable the use of stanniocalcin in the detection of lung cancer, because Olsen et al mentions a whole host of potential uses for stanniocalcin. Applicant concludes that the specific embodiments of detecting metastatic lung cancer are included in a whole "laundry list" of disorders or ailments and enabling support, cannot be found in the disclosure. This has been considered but not found persuasive. Olsen et al state [0427] that diseases associated with increase cell survival or the inhibition of apoptosis that could be detected using polynucleotides include many solid tumors and lung cancer. In paragraph [0428] Olsen et al state that additional diseases or conditions associated with increased cell survival that could be detected using stanniocalcin polynucleotides include metastasis of malignancies including leukemias and solid tumors comprising lung carcinoma and small cell lung carcinoma. Thus it is clear from the disclosure of Olsen et al that lung cancer and metastatic lung cancer and small cell lung cancer are detectable by using the polynucleotides of stanniocalcin. It is noted that Olsen et al do not illustrate by specific examples how to detect cancer by using the stanniocalcin polynucleotide. However, the use of polynucleotides to detect hydridization complexes, wherein said hybridization complexes are indicative of a level of expression of a particular polynucleotide within a sample, and wherein the level of expression of said tumor polynucleotide is indicative of a cancerous state are well known in the art. Section 2164.01 of the MPEP states

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of Mineral Separation v. Hyde, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). See also United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."). A patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies , Inc ., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). Determining enablement is a question of law based on underlying factual findings. In re Vaeck, 947 F.2d

488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

The specification of Olsen et al correlates the stanniocalcin polynucleotide with various types of cancers including lung cancer and metastatic cancers. Said specification does not demonstrate a quantitative relationship between the level of expression of stanniocalcin which is indicative of a cancerous state, nor does it disclose that said stanniocalcin is upregulated or downregulated in said cancerous state. However, it would not be undue experimentation to determine to what extent the expression level of stanniocalcin differed between cancerous tissues and normal tissues. To make said determination, one of skill need only the tumor samples and normal tissue samples from which to obtain polynucleotides and nucleic acid probes which hybridize to the stanniocalcin polynucleotide. Olsen et al provide the sequence of the stanniocalcin polynucleotide, however, said polynucleotide was disclosed prior to Olsen et al. Methods of detecting or diagnosing the presence of cancers or tumors by means of detecting a cancer or tumor-associated polynucleotide are well known in the art as exemplified by Cohen et al (US 6,110,675, claims 1-9), or Hillman et al (US 6,020,478, claim 9) which demonstrate a high level of skill in the art regarding the detection of cancer associated polynucleotides at the time of filing. Thus, it would not be undue experimentation to detect cancer and tumors by using the stanniocalcin polynucleotide because Olsen et al identified the stanniocalcin as a cancer associated polynucleotide , Olsen et al identified the specific cancers and specific tumor types [0382, 0400, 0402, 0421, 0423, 0427, 0428], thus giving a considerable amount of guidance as to the specific cancer associated tissues involved and the identification of stanniocalcin as the specific cancer associated polynucleotide target. the polynucleotide sequence of stanniocalcin was known in the art and methods of detecting tumor-associated polynucleotides were art recognized.

Thus while Olsen et al did not give any working examples regarding the detection of cancer and metastatic cancer by the stanniocalcin polynucleotides, the examiner contends that it is well within the purview of one of skill in the related arts to do some further experimentation in order to carry out the method disclosed by Olsen et al.

4. The rejection of claims 1-5 and 12 under 35 U.S.C. 103(a) as being unpatentable over Olsen et al (Pub No. US 2002/0042372 A) in view of Sobol et al (U.S. 5,543,296) as evidenced by the alignment of the instant amino acid sequence of SEQ ID NO:3 and polynucleotide of Sequence 1 is maintained for reasons of record.

Claim 3 is drawn to a method of staging cancer in a patient having cancer comprising: determining Lng108 levels in a sample of cells, tissues or bodily fluids from a patient; and comprising said Lng108 levels with the Lng108 levels in the cells, tissues or bodily fluids of a normal human control, wherein an increase in the Lng108 levels in said patient is associated with a cancer which is progressing and a decrease in the Lng108 levels is associated with a cancer which is regressing or in remission, and wherein Lng108 comprises a polynucleotide of SEQ ID NO:1 or 2, a polynucleotide which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO:1 or 2, or a protein expressed by a polynucleotide sequence of SEQ ID NO:1 or 2. .

Claim 4 is drawn to a method of monitoring cancer in a patient for the onset of metastasis comprising identifying a patient having cancer that is not know to have metastasized; periodically determining levels of Lng108 levels in samples of cells, tissues or bodily fluids from said patient; and comparing the periodically determined levels of Lng108 with the levels of Lng108 for the cells, tissues or bodily fluid or a normal human control; wherein an increase in any one of the periodically determined Lng108 levels in the patient versus the control is associated with a cancer which has metastasized and wherein Lng108 comprises a polynucleotide of SEQ ID NO:1 or 2, a polynucleotide which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO:1 or 2, or a protein expressed by a polynucleotide sequence of SEQ ID NO:1 or 2. Claim 5 is drawn to a method of monitoring a change in stage of cancer in a patient comprising: identifying a patient having cancer that is not know to have metastasized; periodically determining levels of Lng108 levels in samples of cells, tissues or bodily fluids from said patient; and comparing the periodically determined levels of Lng108 with the levels of Lng108 for the cells, tissues or bodily fluid or a normal human control; wherein an increase in any one of the periodically determined Lng108 levels in the patient versus the control is associated with a cancer which is progressing in stage and a decrease is associated with a cancer which is regressing in stage or in remission, and wherein Lng108 comprises a

polynucleotide of SEQ ID NO:1 or 2, a polynucleotide which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO:1 or 2, or a protein expressed by a polynucleotide sequence of SEQ ID NO:1 or 2. Claim 12 embodies the methods of claims 1, 2, 3, 4 and 5 wherein the cancer is lung cancer. The specific embodiments of claims 1 and 2 are set forth above.

The enclosed alignment indicates that the instant amino acid sequence of Lng108, SEQ ID NO:3, is encoded by Sequence 1 of Olsen et al. Olsen et al terms the amino acid encoded by Sequence 1 as stanniocalcin.

Olsen et al teach a method for detecting lung cancer and metastatic lung cancers and other cancers and metastatic cancers comprising the detection of the Lng108 polypeptides and/or polynucleotides, for the reasons set forth above. Olsen et al do not specifically teach method steps which recite the staging of cancer or method steps which are repeated over time to determine the progression of cancer.

Sobol et al teach that recent advances in cancer therapeutics have demonstrated the need for more sensitive staging and monitoring procedures to ensure initiation of appropriate treatment, to define the end points of therapy and to develop and evaluate novel treatment modalities and strategies, but that conventional methods to detect distant metastases do not have adequate sensitivity (column 1, lines 27-41). Sobol et al teach that because of this lack of sensitive method for detecting metastases, 25% to 30% of patients having non-small cell lung cancer who are classified as having Stage I disease actually have metastatic lesions that are not detected and that these individuals are nor cured by primary tumor resection (column 1, lines 42-67). Sobol et al teach the necessity of adequate staging methods for the management of both non-small cell lung cancer and small cell lung cancer (column 2, lines 1-18). Sobol et al teach that small cell lung cancer patients generally have metastatic disease at the time of diagnosis. Sobol et al teach that current staging procedures cannot distinguish SCLC patients who will have earlier relapses despite achieving initial complete remission, because most patients who have initial complete remission have minimal residual disease which cannot be detected by conventional methods and that more sensitive methods are needed to detect metastases and thereby identify patients at high risk for early tumor recurrence who may benefit from additional systemic therapy.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to monitor patients having cancer, and especially lung cancer over time for the presence of Lng108 in cells, tissues and bodily fluids in order to stage the progress of the cancer. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Sobol et al on the necessity of monitoring for the presence of metastases in patients having lung cancer in order to provide such patients who develop metastatic lesions with appropriate systemic therapy, beyond that of primary surgical resection.

5. Applicant argues that the rejection under 103(a) is faulty because Olsen et al is not an enabling disclosure, and Sobol et al fails to remedy the deficiencies of the primary reference of Olsen et al because the teachings of Sobol et al are unrelated to stanniocalcin. this is unpersuasive for the reason set forth above, wherein the examiner maintains that the Olsen et al reference is an enabling disclosure. Applicant argues that even if the disclosure of Olsen et al were enabling, the combination of Olsen et al and Sobol et al is at beast only "obvious to try" which has been deemed by the court of Appeals for the Federal Circuit as improper grounds for a rejection under 35 USC 103(a). This has been considered but not found persuasive. Olsen et al specifically teaches the detection of metastatic lung carcinoma and metastatic small cell lung carcinoma (paragraph [0428] especially lines 4-5, 14, 28-29). Sobol et al teaches that a sensitive monitoring system for lung cancer patients is necessary because many patients have metastatic tumors which go undetected . Sobol et al particular point to patients having small cell lung carcinoma who frequently have metastatic lesions which go undetected and therefore untreated after surgical resection of the primary tumor. The examiner maintains that it would be prima facie obvious to use the stanniocalcin polynucleotide in the detection of metastatic lung cancer and the monitoring of lung cancer patients because the stanniocalcin polynucleotide was taught to be a lung cancer specific polynucleotide and useful for the detection of metastatic lung cancer by Olsen et al, and Sobol et al teach the necessity of detecting metastatic lung cancer and monitoring patients for metastatic lung cancer . One of skill in he art would be motivated to monitor patients for metastatic lung cancer so that said patients may be given the proper treatment.

6. All other rejections and objections are withdrawn in light of applicants amendments.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
9/30/03